UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/759,777	01/12/2001	Maria Isabel Gonzalez	5771-P1-01-BD	9663

7590 02/12/2003

Warner-Lambert Company
2800 Plymouth Road
Ann Arbor, MI 48105

EXAMINER
HUI, SAN MING R

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 02/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/759,777	GONZALEZ ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2002 and 16 July 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-10,14 and 16-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-10,14 and 16-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendments filed October 30, 2002 have been entered.

The cancellation of claims 2-3, 11-13, and 15 is acknowledged. The addition of claims 24-46 is acknowledged.

Claims 1, 4-10, 14, and 16-46 are pending.

Claims 16 and 43 are objected to because of the following informalities: the use of abbreviation in claim 16: "NO" and claim 43, line 2: "**VIP** enhancer", is considered improper. Appropriate correction is required.

Because of the cancellation of claims 12 and 13 and the amendments filed October 30, 2002, the outstanding rejections under 35 USC 112, second paragraph are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-10, 14, and 16-46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are drawn to a method of "preventing sexual dysfunction". In the instant specification, there is no guidance as to how one of skilled in the art to select an appropriate bombesin receptor antagonist in

use for "preventing the sexual dysfunction". The instant specification only discloses embodiments to "treat" sexual dysfunction rather than "prevent" it. Working examples in demonstrating the preventive efficacy of bombesin antagonist in the method of preventing sexual dysfunction are not disclosed in the instant specification. It is well-known in the art that sexual dysfunction can be caused by various different etiologies (See Merck Index reference of record) and none of those etiologies are known to the skilled of artisan to be directly associated with bombesin receptor. Without specific guidance in the specification, undue experimentation would be required for one of skilled in the art to ascertain the appropriate embodiment to "prevent sexual dysfunction".

Claims 36 and 46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The term "neurotransmitter modulator" recited in the claims encompasses selective serotonin reuptake inhibitor (SSRI). However, SSRI are known to cause sexual dysfunction. Therefore, claims 36 and 46 are not enabled for the full scope as claimed. There are only limited numbers of neurotransmitter are set forth in the instant specification. Without any specific guidance on how to select and ascertain the appropriate embodiments to practice the instant invention, undue experimentation would be required for one of skilled in the art to ascertain the appropriate embodiment to practice the instant invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-10, 14, and 16-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expression "a method of ... preventing sexual dysfunction ... subject ... liable to suffer therefrom" recited in claim 1 renders the claims indefinite as to the host encompassed thereby. It is not clear what subjects would be encompassed by the claims because there is not known how to predict sexual dysfunction before it happens.

The expression, "a method of preventing sexual dysfunction" in claim 1, line 1, renders the claims indefinite as failing to clearly set forth the metes and bounds of the patent protection desired. Examples of how and when to prevent sexual dysfunction are not set forth in the specification. Absent such exemplication, the skilled artisan could not establish the identity of those situations wherein prevention of sexual dysfunction would be effected. Furthermore, it is unclear as to the degree of prevention (e.g., total prevention, some prevention, probable prevention, total prevention in most cases...etc.) herein because the specification does not disclose the extent of prevention achieved.

The expression "a compound that promotes production of NO" in claim 16 renders the claims indefinite as to the compound encompassed thereby. It is unclear

what compounds would be considered as "a compound that promotes production of NO".

The expression "an angiotensin-2 receptor" in claims 33 and 44 are not clearly understood. It is apparent the term is intended to refer to "an angiotensin-2 receptor antagonist". Is it is so, appropriate correction is recommended.

The term "VIP enhancer" in claim 43 renders the claim indefinite as to the compounds encompassed thereby.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-9, 24-28, and 37-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Howell et al. (WO 98/07718).

Howell et al. (WO 98/07718) teaches a method of treating and/or preventing depression employing a oral pharmaceutical composition/dosage form comprising non-peptide bombesin receptor antagonists (See particularly, abstract, page 10 and claims 11-12).

Claims 1, 4-9, 24-28, and 37-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Hurel et al., reference of record.

Hurel et al. teaches that bombesin-like peptide antagonists have vasoactive properties, see page 1243.

The method of administering a bombesin antagonist to a patient, whom is liable to suffer, but without sexual dysfunction, will inherently prevent sexual dysfunction in such patient.

Applicants' attention is directed to *Ex parte Novitski*, 26 USPQ2d 1389 (BOPA 1993) illustrating anticipation resulting from inherent use, absent a *haec verba* recitation for such utility. In the instant application, as in *Ex parte Novitski*, supra, the claims are directed to preventing a malady or disease with old and well known compounds or compositions. It is now well settled law that administering compounds inherently possessing a protective utility anticipates claims directed to such protective use. Arguments that such protective use is not set forth *haec verba* are not probative. Prior use for the same utility clearly anticipates such utility, absent limitations distancing the proffered claims from the inherent anticipated use. Attempts to distance claims from anticipated utilities with specification limitations will not be successful. At page 1391, *Ex parte Novitski*, supra, the Board said "We are mindful that, during the patent examination, pending claims must be interpreted as broadly as their terms reasonably allow. *In re Zletz*, 893 F.2d 319, 13 USPQ2d 1320 (Fed. Cir. 1989). As often stated by the CCPA, "we will not read into claims in pending applications limitations from the specification." *In re Winkhaus*, 52 F.2d 637, 188 USPQ 219 (CCPA 1975).". In the

instant application, Applicants' failure to distance the proffered claims from the anticipated prophylactic utility, renders such claims anticipated by the prior inherent use.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4-10, 14, and 16-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Howell et al. (WO 98/07718) and Hurel et al. in view of Merck Manual and sildenefil prescribing information, references of record.

Howell et al. (WO 98/07718) teaches a method of treating and o/or preventing depression employing a oral pharmaceutical composition/dosage form comprising non-peptide bombesin receptor antagonists (see particularly, abstract, page 10 and claims 11-12).

Hurel et al. teaches that bombesin-like peptide antagonists have vasoactive properties (see page 1243).

Howell et al. (WO 98/07718) and Hurel et al. taken together do not particularly teach the employment of bombesin-like peptide and/or non-peptide antagonists in a method of treating sexual dysfunction. Neither do they teach the combination of vasodilators, neurotransmitter antagonists and/or agonists or a horrmone like compound in its method of treating sexual dysfunction.

Merck Manual teaches depression, low testosterone level and vascular abnormalities as causes of sexual dysfunction (see pages 1575 and1577-78).

Sildenafil is a known PDE5 inhibitor vasodilator employed in the treatment of sexual dysfunction (see pages 5-6).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ bombesin-like peptide and/or non-peptide antagonists in a method of treating sexual dysfunction. It would also have been obvious to combine

the bombesin receptor antagonist with vasodilators, neurotransmitter antagonists and/or agonists or a hormone like compound in a method of treating sexual dysfunction.

One of ordinary skill in the art would have been motivated to employ bombesin-like peptide and/or non-peptide antagonists in a method of treating sexual dysfunction because (1) they are known to be employed in methods of treating depression which is known to be an underlying cause of sexual dysfunction; (2) they are known to be vasoactive which are known to be useful in treating sexual dysfunction. One of ordinary skill in the art would have also been motivated to combine the bombesin receptor antagonist with vasodilators, neurotransmitter antagonists and/or agonists or a hormone like compound in a method of treating sexual dysfunction since they are all known to be useful in treating sexual dysfunction. Combining agents that are known to be useful for the same purpose in a combination composition to be used for the same purpose is known to be within the skill of the artisan and therefore obvious, see *In re Kerkhoven* 205 USPQ 1069.

Claims 24-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Howell et al. (WO 98/07718) and Hurel et al. in view of Merck Manual and sildenefil prescribing information, references of record as applied to claims 1, 4-10, 14, and 16-23 above, and further in view of Leiblum (International Journal of Impotence Research, 1998; 10(Suppl 2): S104-S106), Levin (Exp. Clin. Endocrinol., 1991;98(2):61-69), Gioco et al. (US Patent 5,565,466).

Leiblum teaches different sexual disorders are affected by either mood disorder such as depression, which would reduce the desire of sexual activities, or vascular factors such as decreased vaginal lubrication which can cause pain during intercourse and female sexual arousal disorder (see particularly page S105, col. 1, second paragraph – col. 2 and page S106, col. 1).

Levin teaches VIP can increase the vaginal lubrication and induce arousal in female patients (see particularly the abstract).

Gioco et al. teaches a method of modulating the excitory phase of male and female sexual response using vasodilating agents such as phentolamine, yohimbine, α-adrenergic vasodilator, and imipramine (See col. 12, line 11 to col. 13, line 31, 45,a nd 66, Examples 3 and 4; also particularly claims 14 and 17).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the herein secondary agents with bombesin antagonist in a method of treating sexual dysfunction.

One of ordinary skill in the art would have been motivated to combine the herein secondary agents with bombesin antagonist in a method of treating sexual dysfunction because various sexual dysfunction are known to be affected by various factors such as depression and vascular. Combining the herein claimed secondary agents, which are known to correct and treat the underlying conditions that negatively affect sexual activities individually, with bombesin antagonist into a single composition for the very same purpose would be obvious (see *In re Kerkhoven* 205 USPQ 1069), absent evidence to the contrary.

Response to Arguments

Applicant's rebuttal arguments filed July 16, 2002 regarding the rejections under 35 USC 102 have been fully considered but they are not persuasive. Please note the claims are drawn to every patient suffered from or liable to suffer from sexual dysfunction. Therefore, the amendments to the claims actually draw the claims closer to the cited prior art instead of distinguish itself from the cited prior art.

Applicant's rebuttal arguments filed July 16, 2002 averring antidepressant having side effect on sexual dysfunction have been considered, but are not found persuasive. Please note that not all antidepressant cause sexual dysfunction. Only certain classes of antidepressant will cause sexual dysfunction, such as SSRI, and the newer generation of tricyclic antidepressants. Absent any evidence that Bombesin antagonist will interact those neurotransmitter systems, one of ordinary skill in the art would still be motivated to employ bombesin antagonist to treat depression and thereby treating sexual dysfunction secondary to depression.

Applicant's rebuttal arguments filed July 16, 2002 averring antihypertensive agents could cause sexual dysfunction have been considered, but are not persuasive. Applicant cited captopril as an example of antihypertensive, which could cause sexual dysfunction. However, the sexual dysfunction does not caused by the direct vasodilating effect of captopril. Bombesin antagonists do not interact with the angiotensin systems as captopril does. Therefore, absent any evidence that Bombesin antagonist will elicit similar mechanism of action as captopril, one of ordinary skill in the

art would still be motivated to employ bombesin antagonist as a vasodilator to treat sexual dysfunction.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (703) 305-1877. The fax phone numbers for the organization where this application or proceeding is assigned

are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
February 7, 2003

SREENI PADMANABHAN
PRIMARY EXAMINER 2/8/03